THE CANCER LETTER

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ETHICS COMMISSION TO CONTINUE CONSIDERATION OF COMPENSATION FOR INJURED RESEARCH SUBJECTS

The President's Commission for the Study of Ethical Problems in Medicine & Biomedical & Behavioral Research has asked for a detailed ethical and moral analysis of the question of compensation for persons injured as a result of participation as research subjects in clinical trials.

Commission members determined they needed the ethical and moral

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In Brief

NO SUCH THING AS PREMATURE DATA, FISHER SAYS— ONLY IMMATURE EVALUATION, PREMATURE APPLICATION

SOME GEMS from Bernard Fisher's Karnofsky lecture (which were not included in the report on the lecture in last week's ***Cancer Letter***): "There is no such thing as premature data; only immature evaluation and premature application. . . . We must invest not in surgical oncology, radiation or medical oncology, not in clinical or basic research, not community physicians, not cancer centers, but in talented people. . . . The prospective randomized trial mechanism is one of the important scientific advances of this century for the study of the biology of cancer. It is the most effective method available for transferring medical practice from an art to a science. I am saddened by those who demean it and consider it not a research effort but an administrative endeavor used to test unimaginative treatment regimens. . . . I am concerned by the psychopathic hostility directed toward the investigator from all fronts, particularly if he or she should be so unfortunate as to be productive." . . . **DAVID GOLDENBERG**, who has been executive director of the Ephraim McDowell Community Cancer Network since it was founded in 1975, has resigned to "return full time to cancer research and other scholarly pursuits." He has been on sabbatical leave at NCI and will remain as professor of pathology at the Univ. of Kentucky. . . . **NATIONAL TOXICOLOGY** Program Board of Scientific Counselors will follow the meeting June 27 to review bioassay reports with another the next day to develop recommendations for a permanent mechanism to perform that review. A progress report also will be heard from the Chemical Nomination & Selection Subcommittee. The June 27 meeting will be at HHS Switzer Bldg., 330 C St. SW in Washington; the June 28 meeting at NIH Bldg 31 Room 10. . . . BREAST CANCER Task Force will meet July 28-29 to hear an overview of the Breast Cancer Program. The meeting will be in NIH Bldg 1 Wilson Hall, 8:30 a.m. both days, all open. . . . **NEW GRANT** application form PHS 398 is now available from NIH-DRG, Office Services Branch, Bethesda, Md. 20205. NIH will accept only the new forms starting with the October-November receipt dates.

COMPENSATION ISSUES INCLUDE DEFINITION OF INJURY, PAYMENT LIMITS, INSURANCE

(Continued from page 1)

analysis after hearing presentations on the various issues involved at their recent meeting in Washington D.C. The next meeting is scheduled for July 11-12, also in Washington; the agenda has not yet been determined.

Excerpts from the minutes of the meeting follow:

Consideration of compensating subjects injured in research began with an effort to obtain data on the incidence of such injuries. Mark Novitch, acting deputy commissioner of the Food & Drug Administration, testified that the agency has had difficulty defining what constitutes an "injury," or an "adverse effect."

Novitch described the drug approval process and the requirement for reporting information on adverse reactions. He said that there is a very low incidence of recorded adverse effects on subjects who participate in studies on investigational drugs.

In response to the Commission's inquiry as to whether FDA has a system that records the number and types of injuries to research subjects, Novitch explained that reports of adverse effects are maintained in individualized files for a particular drug trial. He said that no centralized system exists which would provide cumulative figures.

Commission member Albert Jonsen suggested that one definition of "research" might make eligible for compensation persons injured as a result of using drugs for purposes other than those for which they have been approved by FDA. He also wondered whether "control" subjects who receive placebos would be counted as "injured" if their health did not improve as much as subjects receiving experimental drugs, devices or procedures in the same experiment. He suggested that ethical standards might be adopted for these situations.

Commission Chairman Morris Abram inquired about the potential effect on research of informing the subject that financial compensation would or would not be available.

Charles McCarthy, director of the Office for Protection from Research Risks in the Dept. of Health & Human Services, stated that alleged violations of compliance with regulations are investigated, although he acknowledged that his office does not know from where inquiries originate. This is because alleged violations of compliance are often made by telephone or presented by persons who request that their identity remain confidential. When such inquiries are made, site visits occasionally take place. However, only two site visits were made in FY 1979 and only three have been made thus far in FY 1980.

McCarthy said there is no centralized file of adverse effects within the department, and that he did not see that such a file would be advantageous. He said that many adverse effects can be anticipated since the vast majority of prescription drugs and many devices cause certain negative side effects in some individuals. He noted that regulations require IRBs to be notified of any unanticipated problems involving risk to subjects. A "general advisory" notice goes out from the OPRR to research institutions or individual investigators only if the injury itself was unanticipated or if the frequency or severity of the anticipated injury was greater than expected. As a result of this policy, McCarthy noted that one advisory had been sent from his office in the previous 18 months.

McCarthy added that few if any injuries would qualify for compensation under the definition of compensable injuries suggested by the HHS Secretary's Task Force. He suggested that the Commission would provide a useful function by offering some guidance to the department on what constitutes an adverse effect for purposes of reporting and record-keeping.

Alexander Capron, executive director of the Commission, observed that the incidence of injuries reported by researchers is far below what would be expected on the basis of experience with patients. This suggests either that investigators are "incredibly lucky or incredibly careful" or that injuries are not all being reported. The absence of reports of adverse consequences may occur because department regulations required reporting only "unanticipated" harm.

Commission member Renee Fox argued for a compensation model which takes probability of injury into account. Commission member Arno Motulsky concurred, but cautioned that society owes some form of compensation to injured subjects regardless of probability considerations. He urged that a solution be found which does not incorporate excessive regulation.

Staff member Barbar Mishkin outlined the studies which have been initiated or are planned regarding compensation of injured research subjects.

The Commission heard testimony on the insurance issue from George Bernstein, formerly Federal Insurance Administrator and now a lawyer in private practice with a speciality in insurance law. Bernstein was skeptical about whether private companies would ultimately be willing to write insurance solely for research on human subjects, although they may be willing to provide it as part of a package to institutions with general liability coverage. He believes that private insurers doubt that the Task Force Report of 1977 was based on adequate statistics about injuries. He also equated the insurers' likely reaction to compensation insurance with their reluctance to take on medical malpractice insurance. A difficult aspect to

the formulation of any private insurance plan will be the determination of what ought to be covered.

Abram suggested that claims for compensation might increase if the insurance companies were willing to provide coverage, and that the very small number of claims may be related to the fact that most insurance companies do not provide compensation. Bernstein agreed, noting that claims from swine flu and black lung injuries rose dramatically once compensation was made available.

Bernstein described the rider provided by Aetna for research injuries under its general insurance for the Univ. of Washington, which paralleled the worker's compensation level of benefit in the state. (Motulsky explained that the university subsequently decided to self-insure when the premiums for the general liability policy got too high.) Bernstein suggested that Aetna was unique in its willingness to take on this coverage and that this was not exemplary of an industry wide position.

Stanley Jones, a consultant on health policy, shared Bernstein's belief that administrators would likely be willing to take on the provision of insurance for injured research subjects, but that the costs of such action might be prohibitive. He suggested that the fundamental problem is how to limit risk in order to make costs more projectible.

Jones said that he examined the following questions in his analysis of the issue: Who is eligible for compensation? How do you determine eligibility? How much do you compensate? How do you administer the program? What will its cost be?

With respect to why costs are rising for federal compensation programs, Jones offered several primary reasons—widened awareness among employees of the benefits; increased benefits due to judicial and congressional action; and the medical and legal difficulties in defining causation such that entire conditions are essentially covered.

Abram suggested three models regarding compensation for injured workers—one in which the injured person receives no compensation due to the assumed risk inherent in the job; a second in which he or she is compensated a statutory amount for specific physical injuries (e.g., the loss of a limb); and a third in which compensation takes into account pain and suffering and loss of future earning power. He rejected the first option, but left open the latter two for discussion.

Jones added that the current nonavailability of compensation distorts the true reading with respect to the number of claims that might be filed once a compensation program is in place and made public. Abram noted that it is often difficult to determine the cause of a specific injury. As a negligence lawyer, he found that people often claim injury to the neck and coccyx, which are particularly difficult to diagnose and verify.

Staff member Alan Weisbard reviewed the staff's preliminary outline for the report on compensation of injured research subjects. Commission member Anne Scitovsky warned that the Commission should distinguish between altruistic research subjects and patients who take part in experiments out of which they expect some therapeutic benefit. She rejected the idea of compensation for the latter category. Motulsky agreed, explaining that a clear policy distinction should be made between therapeutic and nontherapeutic research. Commission member Donald Medearis disagreed, saying that all people who participate as research subjects contribute to the public good, and therefore deserve consideration for compensation.

Noting that some attention was to be paid to compensation programs in other countries, Fox reminded the Commission of the importance of varying cultural attitudes toward risk in drawing analogies.

Capron asked for a sense of the Commission on whether it wanted to pursue a detailed ethical and moral analysis of the compensation issue or would be satisfied with a summary of the reasoning of the 1977 Task Force Report on Compensation. Arguments in favor of both alternatives were voiced, although a consensus seemed to emerge for a full explanation of the ethical rationale for compensation.

INTERFERON "HYSTERIA OUT OF HAND," ASCO WARNS AGAINST EXPECTING BENEFIT

The American Society of Clinical Oncology has taken the unusual, if not unprecedented, step of issuing a formal statement warning against overexpectations for a cancer therapeutic agent—in this case, interferon.

"We were disturbed by the mass hysteria about interferon among cancer patients," Charles Moertel, director of the Mayo Comprehensive Cancer Center and immediate past president of ASCO, told *The Cancer Letter*. "It has gotten out of hand. Every cancer patient I have seen for months has asked about interferon."

Moertel said the following statement was approved by ASCO officers and the Board of Directors, including new President Emil Freireich:

"The officers and Board of Directors of the American Society of Clinical Oncology, based on results presented for scientific scrutiny at the Society's meeting concluded on May 28, wish to express caution regarding possible benefits of interferon treatment for patients with cancer. Interferon, as currently prepared and used, is a toxic drug that may produce side effects such as chills, fever, lowered blood pressure and depression of blood counts. Favorable therapeutic results for patients in more recent experience have been far less impressive than those originally publicized. Any benefit achieved has

frequently been equivocal in nature and very transient. There is no evidence or even remote suggestion that interferon may be curative for advanced cancer.

"At this time there is no acceptable evidence that interferon is capable of extending life expectancy of cancer patients regardless of type or stage of malignant disease.

"There are many other new approaches currently under investigation that have produced results equal to or more favorable than interferon.

"Interferon is a natural product of human cells, and its mechanism of action may be different than other antitumor substances. We would recommend, however, that considerably more basic and well controlled study be conducted on interferon before it is accorded any status as a treatment of value for cancer."

NEW PUBLICATIONS

"Self Examination After Breast Cancer Surgery," by Dorothy Hollis, RN; edited by Carol Golden, published by Ephraim McDowell Community Cancer Network, 915 S. Limestone, Lexington, Ky. 40536. Up to five copies free; over five, 10 cents per copy; over 100, five cents per copy.

"A Comprehensive Guide for Cancer Patients and Their Families," by Ernest and Isadora Rosenbaum, Bull Publishing Co., P.O. Box 208, Palo Alto, Calif. 94302, $11.95 paperback, $19.95 clothbound.

"Breast Exams: What You Should Know," by NCI's Office of Cancer Communications. Multiple copies free from OCC, NCI, Bethesda, Md. 20205.

"Public Education About Cancer—Recent Research and Current Programs," edited by Patricia Hobbs. Published by UICC, 3 rue du Conseil-General, CH 1205, Geneva, Switzerland. 10 Swiss francs plus postage.

"Conversation After Mastectomy," 30 minute tape of an informal discussion with postmastectomy patients at Memorial Sloan-Kettering Cancer Center, directed by Guy Robbins, provided as a professional service by Stuart Pharmaceuticals. Available free from NCI, Office of Cancer Communications, Bethesda, Md. 20205.

ONS GROWING IN SCIENTIFIC PROGRAM AS WELL AS IN MEMBERSHIP INCREASE

The Fifth Annual Congress of the Oncology Nursing Society was a demonstration of the growing strength of the organization not only in numbers (with more than 2,300 members), but also in the scope and depth of the scientific presentations at the meeting.

The Congress proceedings included abstracts of 178 papers, 50 of which were presented at the Congress. Selected examples follow:

INFORMATION ON RADIATION THERAPY IN EARLY BREAST CANCER—Lydia Greiner, Clare Weiler, Univ. of Pennsylvania

Between August 1977 and September 1979, 66 patients with early carcinoma of the breast were treated with definitive irradiation as opposed to mastectomy at the referral of these patients to the radiation therapist. Patterns seemed to be quite varied. Since this alternative to mastectomy is not well known to the public, a study was undertaken to determine the actual referral patterns. Fifty of the patients were interviewed. The patients were questioned about their knowledge of radiation therapy in general and specifically relative to breast cancer, both prior and after a definitive diagnosis had been established. Virtually none of the patients had any significant knowledge about the common belief that radiation therapy is reserved for "hopeless" cases. Most of these beliefs persisted to some degree following some mention of radiation therapy by the referring physician. Patients were also questioned about the origin of their referral to the radiation therapist. Fifteen patients were referred by their physicians shortly after diagnosis, having had radiation therapy presented as an acceptable alternative. The remaining 35 patients were either told nothing about an alternative to mastectomy or that radiation therapy was not an acceptable alternative. These patients persisted, however, and were referred reluctantly by their physicians or self referred by various articles in lay magazines, press, or by patients who had already had such treatment. We suggest that nurses, as health educators, could make a significant impact on the availability of information regarding alternatives to mastectomy.

CHEMOTHERAPY FOR THE HOMEBOUND ONCOLOGY PATIENT—Geraldine Hunter, Susan Johnson, Visiting Nurse Assn., Abington, Pa.

As a Visiting Nurse Assn., our agency believes that many of the most specialized needs of the homebound patient can now be met by skilled, appropriately trained nurses. Initiating intravenous therapy in the home has proven successful. This led us to pursue an even more specialized level of care to include the cancer patient.

Staff RNs with previous experience in critical care nursing and IV therapy attended an 80 hour inservice at American Oncologic Hospital. This included a 40 hour practicum preparing and administering parenteral chemotherapeutic agents to outpatients with various types of cancer. Under the guidance of the chief pharmacologist there and by utilizing procedures and policies obtained from other VNAs, a list of drugs was compiled that would demonstrate the widest margin of safety for use in the home. Establishing goals and criteria for referral of homebound oncology patients who required administration of chemotherapeutic agents was accomplished. This service is offered to those patients with whom a competent person is in attendance. A great deal of patient and family instruction has contributed to attaining our goal. We are currently in the process of informing the physicians and the communities whom we serve of our new areas of specialization. Oncology nursing is a vital aspect of homecare. Debilitation and deterioration often go hand in hand with cancer. It is crucial that skilled professional nurses are prepared to meet the changing needs of these patients.

OUTPATIENT INTRAVENOUS CHEMOTHERAPY DELIVERED BY PORTABLE INFUSION PUMPS—JoAnn Bowen, Kathy Marts, K.B. McCredie, M.D. Anderson Hospital

Treatment strategies for cancer patients frequently require long term intermittent IV therapy that necessitates patient hospitalization an average five days/month for a year or longer. We have previously demonstrated the safety and reliability of silicone central venous catheters to remain indwelling in many of these patients for the duration of their therapy.

Between courses of IV therapy, catheter patency is maintained by heparin lock. These factors have led to our investigation of portable infusion pumps for delivery of outpatient IV therapy.

These devices allow delivery of drugs on a continuous basis over controlled time intervals. We have evaluated three portable infusion pumps and two (the Cormed and the Auto-Syringe) have been used in our pilot project. Reliability of the Cormed Pump is pending further studies. The Auto-Syringe pump has proven accurate ±2 percent.

Over a seven month period, 307 outpatients with an indwelling silicone central venous catheter have had IV chemotherapy (including vesicant drugs) delivered by the Auto-Syringe pump for a total of 1,322 hospital days saved. 97 percent finished therapy as ordered. Three percent had therapy interrupted by their doctor, unrelated to technical problems. There were no major complications. These data suggest that this system for delivery of continuous IV chemotherapy on an outpatient basis can be as safe and reliable as the same treatment delivered by conventional IV methods to the hospitalized patient. Advantages include more available hospital beds, cost savings for the patient and minimal disruption of the patient's lifestyle during therapy. Success of the program is based on pump reliability, use of silicone central venous catheters for IV access, extensive patient/family education, and a well trained staff to manage the program.

USE OF BODY STROKING IN PATIENTS EXPERIENCING NAUSEA AND VOMITING WITH INTRAVENOUS CHEMOTHERAPY–Jeanne Valencius, City of Hope National Medical Center

The purpose of the study is to implement and evaluate a body stroking technique on adult medical oncology and surgical adjuvant clinic patients receiving intravenous chemotherapy. The specific objectives of the pilot study are to test whether the group receiving stroking prior to chemotherapy treatment exhibits significantly less nausea and vomiting than a control group, to test whether the group receiving stroking requires significantly fewer needle sticks than the control group, to test the specific procedure and instruments, and to predict responders and nonresponders to stroking.

Preliminary trials on four patients who had problems with GI upset or needle insertion yielded observable relaxation and decreased nausea. This was noted by patients, visitors, and clinic nurses. Twenty consenting patients will be randomized into two groups. Ten experimental patients will receive stroking at two different clinic visits. Ten control patients will receive an interview only followed by stroking during a second clinic visit. Patients will be pre and posttested regarding levels of distress. An impartial nurse observer will be applied by the investigator immediately prior to the treatment. Data analysis will consist of frequency distributions to describe subject population and their responses. Nonparametric statistics will be used to determine differences between treatment and control groups. If the technique is proven effective it may provide a simple, quick, noninvasive, no-cost method of preventing nausea, vomiting, and multiple needle sticks.

THE CONSORTIUM: A MODEL FOR COLLABORATIVE NURSING RESEARCH–Barbara Hansen, Univ. of Michigan

Areas of nursing which must consider the patient as a whole (physiological, socio-economical, etc.) such as oncology nursing, can benefit from the consortium approach to collaborative research among nurses and other health care professionals. The multidisciplinary backgrounds and variety of settings and client populations represented by a consortium group greatly expand the number of variables, the number of subjects and the amount of clinical data that can be obtained in a series of studies.

Advantages of the consortium approach include: a) the systematic measurement of a wide variety of dependent and interactive variables; b) the strategies for conducting simultaneous studies (experimental and descriptive) on a single subject, thus conserving resources and maximizing data; c) consideration of multiple factors, such as cultural-ethnic groups, variations in treatments which may occur in different settings, variations in diagnostic categories and nursing problems and d) the ability to replicate studies or expand studies.

NEEDS OF FAMILIES OF ADULT CANCER PATIENTS–Deborah Welch, Fred Hutchinson Cancer Research Center

Families are often the cancer patient's first line of support but often their emotional and informational needs are not systematically addressed, while they are expected to effectively sustain the ill family member as well as meet many of the patient's physical needs in the home setting. This phenomenon may leave the family feeling anxious, helpless, reluctant or unable to participate in the total patient care effort. Subsequently the continuum of quality patient care may be disrupted as a result of the nurses' ineffectiveness of meeting family's needs.

Cancer nurses can provide better care and assistance to patients and families if needs have been systematically documented through nursing research. Therefore, in order to assess the specific needs of family members, a pilot survey was completed by 30 members of adult cancer patients who were in various stages of illness (initial diagnosis through advancing disease), who had a variety of types of malignancies. The following research questions have guided this exploratory study: What are the needs of families at varying stages of the patient's illness? How do families' needs change as treatment progresses? Do family needs vary particular to the patient's type of malignancy? What nursing interventions do families identify as being helpful throughout the continuum of cancer patient care?

The results of the pilot survey have been analyzed and questionnaire modifications have been made. The final survey is being sent to 100 additional families.

HOW TO TALK TO YOUR DOCTOR ABOUT CANCER–Sandra Wroblewski, Los Angeles

"My doctor doesn't tell me anything." "My doctor ignores my symptoms. He tells me that's nothing to worry about." Chances are, wherever your work setting is, you have heard comments such as these or others like these. How do we, as nurses, respond to these kinds of statements and feelings? Based on the belief that effective communication and trust are the basis for establishing and maintaining a therapeutic relationship, we proceeded with this enormous task.

A public education program was designed to explore the need: for open communication between the doctor and patient, as well as their separate responsibilities as members in the relationship. Issues addressed in the seminar included such topics as the importance of communication in the doctor-patient relationship, the patient's right to informed consent and his right to refuse treatment, the patient's or family's lack of responsibility in communicating what is really bothering them, how much the patient really wants to know, how to ask your doctor about nontraditional therapies, and the control of pain. General fears expressed centered around three main themes–isolation, fear of being abandoned, and mistrust. The major goal of this program was to give the cancer patient and his family the strength to demand the truth and the will to search for satisfying answers to their questions.

LUNG TUMORS AND ECTOPIC HORMONE SYNDROMES–Ada Lindsey, Virginia Carrieri, Barbara Piper, Univ. of California (San Francisco) School of Nursing

Case histories describing clinical manifestations of excess hormone secretion observed to occur concomitantly with certain malignant neoplasms have been reported for over 50

years. More recently with the development of more sensitive and specific assay techniques, it has become possible to detect and document that some nonendocrine tumors produce and secrete hormones or hormone-like substances. If these ectopically produced hormones are biologically active and secreted in excess, over time, the resulting clinical metabolic aberrations become apparent and in some cases these alterations are more immediately life-threatening than the tumor from which the ectopic production is occurring. For this reason, it is imperative that nurses become knowledgeable about the clinical manifestations of ectopic hormone syndromes which occur with some malignant tumors. Two syndromes which are associated with lung tumors will be reviewed; these are the ectopic ACTH secretion and the ectopic parathyroid cortisol and hypercalcemia, respectively.

NURSE'S ROLE IN REGIONAL HYPERTHERMIA–Janet Cook and Jean Pirtle, M.D. Anderson Hospital & Tumor Institute

Hyperthermia for regional treatment of cancer has been under clinical Phase 1–phase 2 study at M.D. Anderson for two years. Various techniques have been employed including ultrasound for smaller superficial lesions or radiofrequency for larger lesions. A wide variety of tumor types has been treated, some in conjunction with radiotherapy or chemotherapy. The overall objective response rate has been encouraging. The complete response rate is 15 percent for ultrasound alone and 60 percent when combined with ionizing radiation.

The entire procedure is performed by nursing personnel. A thermocouple to monitor the temperature is inserted into the tumor followed by the application of a water cooled apparatus to conduct ultrasound or radiofrequency fields. The temperature of the tumor is raised to at least 43 degrees C. Usually the treatments are given for one hour, three times a week for three consecutive weeks depending upon the patient's response. Temperatures are carefully monitored and recorded. The water cooled system prevents skin burning. If pain occurs, medication will be given to relieve discomfort. The patient's physical and emotional comfort must be considered at all times. Keeping accurate records and followup is very important.

This is a new and exciting field for nursing intervention. Technical skills must be utilized and assessment of patient response to this new form of treatment is essential.

NURSING RESEARCH IN A COOPERATIVE GROUP SETTING–Deborah Mayer-Scogna and Connie Henke Yarbro, Southeastern Cancer Study Group

A nursing research study was developed by the Nursing Committee of the Southeastern Cancer Study Group and is the first formal, interinstitutional nursing research within a cooperative group. As such it has set a precedent and may serve as a useful role model.

The purpose of this abstract is to review the development and process of this endeavor. A prospective study was developed to evaluate: 1) the compliance rate of patients entered on an investigational protocol, and 2) the effects of nursing intervention using a structured teaching tool on patient knowledge and compliance. The actual protocol was developed for patients entered into a study of "good risk" breast patients receiving chemotherapy $\pm$ immunotherapy and demonstrated the ability of joint collaboration between a specific disease oriented committee and the nursing committee. Means to monitor compliance rates include: the actual number of patient visits, laboratory tests obtained and quantity of oral medication taken as compared with the requirements of the protocol.

The study involving seven SECSG institutions will span 15 weeks per patient. They will be tested pre and post study to evaluate the effect of the intervention on their knowledge of the disease and treatment. A total of 50 patients will be required to evaluate the study's objectives with a standard error of 10 percent and will take approximately two years to complete. Since the study opened July 1979, 10 patients have been entered.

AN OVERVIEW OF RADIATION THERAPY FOR ONCOLOGY NURSES–Carol Marshall, Indiana Univ. School of Medicine

Oncology nurses must have a fundamental working knowledge of the different treatment methods used in the management of cancer patients. When patients are referred for radiation therapy, it is often the general oncology nurse who is responsible for informing the cancer patient what symptoms and/or side effects he or she may expect from the treatments. A recent survey of 50 general oncology nurses was conducted to determine their knowledge and training in radiation oncology. Surprisingly, 80 percent of the nurses surveyed had little or no knowledge as to side effects or treatment results in patients undergoing radiation therapy. 100 percent of the nurses surveyed indicated a desire to learn more about the general aspects of radiation oncology.

RFA NIH-NCI-DCBD-BCPCB-80-5

Title: *Correlation between microscopic characteristics of primary breast tumors and subsequent patient survival*

Application receipt date: *Oct. 15, 1980*

The Breast Cancer Program of NCI is inviting grant applications to search for parameters based on histological, histochemical, immunohistochemical, or other methods, that would allow more precise prediction of the survival of breast cancer patients.

Screening for breast cancer has found cases at a frequency exceeding incidence figures. It has been suggested that some lesions rarely or never become metastatic. Such lesions would then not be biologically important, as far as patient survival is concerned.

Analysis of the survival data on breast cancer patients has stimulated the hypothesis that the cases include at least two prominent populations, distinguished by a striking difference in relative mortality. On the basis of this analysis, about 40 percent of newly diagnosed cases would die at an exponential rate of about 25 percent per year, while the remaining 60 percent would die at a rate of only about 2.5 percent per year. Even if a significant number of cases dies at rates falling between these two extremes, there is a major difference between the extremes of survival for less than two years, and survival for more than 10 years.

Patients with local breast cancer (no evident lymph node involvement) generally exhibit a lower mortality rate; however, of the patients diagnosed as having regional disease, (i.e., with lymph node involvement), one third also have a low mortality. This survival pattern would be expected if two thirds of the patients with regional disease harbor a "virulent", biologically aggressive form of breast cancer. Women diagnosed with regional breast cancer therefore provide the most promising opportunity for the identification of any possible, characteristic, histological

features that might distinguish those with higher mortality rates.

A number of gross and histological parameters in breast cancer have been used to predict prognosis and estimate survival. These include size and/or contour of the primary lesion, growth rate (motoses or doubling time), histologic type, tumor differentiation (histologic grade and nuclear grade), extent of lymphocytic infiltration, mucin secretion, lipid content, necrosis, lymphatic and/or blood vessel invasion, number of axillary nodes involved with tumor, and histology of the nodes. However, these parameters are not absolute predictors, are subject to individual subjective determination, and depend upon the sampling of the primary lesion for histology and the detail of the pathology review.

The Breast Cancer Program is interested in delineating other parameters (in addition to current gross and histological ones) that might better correlate with prognosis and survival. These parameters should be detectible in tissue specimens fixed by routine pathology laboratory procedures; they could be delineated by histological, histochemical, immunohistochemical, or other methods. If types of regional breast cancer differ in biological aggressiveness, tissues originally obtained at the time of surgery, from patients whose subsequent survival is known could be used to search for features that distinguish them.

Clinical trials on breast cancer have been complicated by the heterogeneity evident in the survival experience of assemblies of treated patients. If this heterogeneity is a reflection of differences in biological behavior of breast cancer, predictable at the time of diagnosis, clinical trials could consider these types separately. It would also be important to ascertain whether these different types of breast cancer differ in epidemiologic characteristics and in etiology.

It is the intent of this RFA to stimulate retrospective studies to search for parameters based on histological, histochemical, immunohistochemical, or other methods, that would permit more precise prediction of the survival of patients with regional or local breast cancer.

It would be desirable to begin the investigation with (but not necessarily confine it to) samples from patients who had lymph node involvement, since differences in survival would be more likely to depend upon differences in the tumor and the host response to it. For such regional breast cancer cases, only duration of subsequent survival (less than two years as opposed to more than 10 years) would select the two groups rather than any differences originally noted at the time of diagnosis. Any variety or combination of tissue slide or specimen preparations could be employed in this search for differences in these two groups. Known epidemiologic risk factors for breast cancer, such as age, menstrual status, reproductive history, family history of breast cancer, etc., should not be considered in the selection of the patients in the two groups, although subsequent correlation with these variables could well be examined.

Applications could be submitted from single or from several collaborating institutions.

It is anticipated that this project need not exceed two years. At least two projects will be funded totaling an approximate direct cost of $100,000 for the first year, and $125,000 for the second year. Project start dates in mid-1981 are anticipated.

Applications must be submitted on form PHS 398, the application form for the traditional research grant. The conventional presentation in format and detail for regular research grant applications should be followed and the points identified under the review criteria must be addressed. The words "Proposal in Response to RFA: Correlation Between Microscopic Characteristics of Primary Breast Tumors and Subsequent Patient Survival" should be typed across the top of the face page of the application. The original and six copies of the application should be sent or delivered to: Application Receipt Office, Div. of Research Grants, NIH, Room 240 Westwood Bldg., 5333 Westbard Ave., Bethesda, Md. 20205.

A copy of the face page should be sent to: Dr. Elizabeth Anderson, Chief, Epidemiology Projects Section, Breast Cancer Program Coordinating Branch, Div. of Cancer Biology & Diagnosis, NCI, Room 4A-46, Landow Bldg., 7910 Woodmont Ave., Bethesda, Md. 20205.

Inquiries concerning this announcement should also be directed to Anderson at this address, phone 301-496-6718.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the contract officer or contract specialist named, NCI Research Contracts Branch, the appropriate section, as follows:
Biology & Diagnosis Section and Biological Carcinogenesis & Field Studies Section—Landow Building, Bethesda, Md. 20205; Control & Rehabilitation Section, Chemical & Physical Carcinogenesis Section, Treatment Section, Office of the Director Section—Blair Building, Silver Spring, Md. 20910. Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

SOURCES SOUGHT

Project No. NCI-CO-04343-S

Title: *Evaluation of the impact of strategic planning on biomedical research (phase 1)*

Deadline: *June 27 for statement of qualification*

Negotiations are to be with the National Academy

of Sciences for this requirement unless other qualified sources are forthcoming. Interested sources are invited to submit five copies of their qualifications to develop several alternative approaches to evaluating the impact of the National Cancer Program Plan. NCI will consider to be qualified those organizations having demonstrable capability to evaluate national biomedical research programs as indicated by previous organizational experience as well as staff expertise and experience. Information submitted should be pertinent and specific to the technical area under consideration for each of the following:

1. Experience—a description of related projects completed or in progress; and
2. Personnel—the name, professional qualifications and experience of key staff members who may be assigned to this project. Any other information that would enhance our consideration and evaluation of your response should be submitted.

Respondents should limit their responses to 10 pages or less. Six copies of the resume of capabilities must be submitted.

Contracting Officer: Hugh Mahanes
Biology & Diagnosis
301-496-5565

SOURCES SOUGHT

RFP NCI-CP-VO-01041-76

Title: *Rapid identification of cell cultures*
Deadline: *June 30 for statement of qualification*

The government has a requirement to continue carrying out a project for the operation of a facility to perform rapid and accurate identification of cell cultures for biological carcinogenesis investigators. Standard techniques are to be used such as: species immunofloresence; interspecies identification of human cells by glucose-6-phosphate dehydrogenase isozyme determination; chromosomal markers; surface markers such as T cell antigens, B & T cell receptors and surface immunoglobulins.

Additionally, the contractor will be required to perform necessary tests to identify a minimum of 350 cultures per year, which would be submitted to the contractor by BCB investigators.

This is not a request for proposal. NCI wishes to receive statements of interest in and qualifications for providing inter- and intraspecies identification of cancer cells in vitro.

The government knows of only one source capable of providing the required services, the Child Research Center of Michigan. Invited to respond are organizations which have capabilities and experiences in performing the work described above.

Qualifications will be evaluated based on an organization's experience as indicated by the following types of information:

1. Past accomplishments of the offeror in operation of a service oriented cell identification operation of similar magnitude.
2. Knowledge of and experience with the biochemical, immunological and cytological techniques required for cell identification.
3. Personnel—formal training and/or relevant work experience.
4. Facilities and equipment.

Cost and price information should not be included. Ten copies of the resume of experience and capability must be submitted.

Contract Specialist: J. Steve Metcalf
Biological Carcinogenesis & Field Studies
301-496-1781

RFP NO1-CP-05689-56

Title: *Resource for long-term animal experiments to study prevention of cancer by retinoids and related materials*
Deadline: *Aug. 8*

Provide the Laboratory of Chemoprevention, Div. of Cancer Cause & Prevention, with an animal resource facility for the evaluation of the efficacy of retinoids and synergistic chemoprevention agents of differing chemical structures to prevent the development of cancer during its preneoplastic period.

A number of target sites for such chemoprevention are anticipated: trachea and bronchi, bladder, breast and esophagus. Appropriate animal models are currently available for these sites. The efficacy of the various chemopreventive agents will have been determined in cell or organ culture studies performed in the Laboratory of Chemoprevention. The protocols for the animal studies will be written by the Laboratory of Chemoprevention, and the necessary carcinogens, retinoids, and other chemopreventive agents will be provided by NCI.

A five-year cost-reimbursement contract is anticipated for effective pursuit of this project.

Contract Specialist: Ann Peale
Carcinogenesis
301-427-8764

The Cancer Letter _Editor Jerry D. Boyd

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